deposits, most probably talc, accompanied by focal proliferative endarteritis were found in the kidney tissue, suggesting intravenous drug addiction in the kidney donor (Figure 1D). Follow-up quantitative Polymerase chain reaction (PCR) for cytomegalovirus (CMV) revealed 65,000 copies/ml. Liposomal amphotericin B, therapy for non-tuberculous mycobacteriosis and ganciclovir were added to the therapeutic regime. The patient’s condition did not improve and despite all efforts, he died 102 days after the transplantation.

This case demonstrates an unfortunate combination of bacterial, fungal and parasitic infections (CMV was reactivation) following kidney transplantation from a living unrelated donor in India. To the authors’ knowledge, 43 cases of post-transplant malaria have been reported [2–4]. During his stay in India, our patient remained in New Delhi and was therefore not exposed to malaria-bearing mosquitoes, so the most likely source of malaria was the allograft. It is highly likely that deep mycosis (A. terreus, Mucor spp.) and M. fortuitum were transmitted by the renal allograft as well. Renal mucormycosis, sharing similarities with our case, has previously been reported in a patient actively using intravenous drugs [5].

Over half of all the renal transplant recipients in tropical countries develop a serious infection at some point in the post-transplant period and 20–40% of them succumb to these infections [1,6,7]. A multitude of factors (unhygienic conditions, hot and humid climate, scanty diagnostic techniques, etc.) contribute to this dismal outcome. In commercial transplantations, the primary objective of the medical team is often profit, and not necessarily the well-being of either donors or recipients.

Conflict of interest statement. None declared.

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Vitamin E and selenium co-supplementation attenuates oxidative stress in haemodialysis patients receiving intra-dialysis iron infusion

Sir,
Parenteral iron administration is a common practice in the era of advanced haemodialysis (HD). A major concern is that the oversaturation of transferrin and subsequent propagation of redox-active iron occurs with the recommended doses of parenteral iron (1–4 mg/kg) [1]. Redox-active iron is a potent pro-oxidant that triggers free-radical chain reaction by the formation of hydroxyl radicals (Fenton reaction) [1–3]. Intravenous iron also increases neutrophil respiratory burst and thus the generation of oxygen radicals [4]. Lipid peroxidation, protein oxidation and DNA damage are the main consequences of this oxidative stress (OxS) [2]. It has been suggested that high cumulative doses of iron may contribute to increased morbidity and mortality among end-stage renal disease (ESRD) patients, through increasing OxS which favours atherosclerosis and is an independent risk factor for cardiovascular mortality [5,6]. Vitamin E and selenium are effective body antioxidants that prevent free-radical formation and halt the damaging free-radical chain reaction once it begins [7–10]. The aim of this study was to assess the efficacy of vitamin E and selenium supplementation on reducing the OxS in HD patients receiving intra-dialysis iron infusion.

Nineteen ESRD patients (mean age, 43 ± 12 years; 11 male and 8 female) on chronic HD were enrolled to this prospective and interventional study. All patients had been undergoing HD twice weekly, while receiving an iron infusion (100 mg iron/5 ml as ferric hydroxide sucrose complex in 10 min via the venous line of the dialysis circuit) 10 min after the beginning of a HD session. Supplements were prepared as capsules, each containing 400 IU vitamin E and 600 µg sodium selenide. All patients received one dose of the aforementioned supplement, 6 h in advance of a scheduled HD session. The same patients were used as the control if they had not consumed the supplement before the HD session. The study was approved by the local research council and ethics committee and informed consent was obtained from patients ahead of the study.

The venous blood samples were drawn immediately before (~10 min after the beginning of HD) and 45–50 min after iron infusion; they were then separated to serum and stored in a refrigerator until biochemical analysis. The serum concentration of malondialdehyde (MDA), an intermediate product of lipid peroxidation [11] was used as a marker of OxS. Briefly, MDA was reacted with thiobarbituric acid by incubating for 1 h at 95–100°C. Fluorescence intensity was then measured in the n-butanol phase using a fluorescence spectrophotometer with excitation and emission at 525 and 547 nm, respectively. The statistical analyses

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were performed by paired t-test using SPSS version 11.0. A P-value less than 0.05 was considered to indicate statistical significance.

We found that the mean serum MDA level was 3.75 ± 1.36 μg/dl before intravenous iron injection, and increased to 4.53 ± 1.93 μg/dl after administration (P < 0.05). However, with prophylactic administration of vitamin E and selenium, the serum MDA level did not change significantly (3.47 ± 1.8 vs 3.76 ± 2.27 μg/dl before and after intravenous iron administration, P > 0.05).

The results of this study show that iron infusion increases serum MDA level and thus intra-dialysis OxS by 21% in haemodialysis patients and that vitamin E and selenium co-supplementation can offset this effect. We did not include a non-iron control group. However, as the blood samples were collected after the beginning of HD session (immediately before the iron infusion) and ~45 min thereafter, the increased OxS reflects mostly the effect of an infused iron. Furthermore, in the study of Roob et al. [1], the serum MDA level remained constant during the course of a dialysis where iron was not infused. In the same study, the MDA showed a marked and rapid increase by 30 min of iron infusion [1].

Selenium functions primarily in the form of the selenoproteins. At least 30 selenoproteins have been identified, including glutathione peroxidase, selenoprotein P, thioredoxin reductase, selenoprotein W, iodothyronine deiodinase and selenophosphate synthetase [9]. Glutathione peroxidase, selenoprotein P and thioredoxin reductase are major components of the body antioxidant system [9]. Vitamin E and glutathione peroxidase function at two different locations within the cell; glutathione peroxidase in the cytosol and vitamin E within the lipid membranes [7,8,10]. Although no synergy has been detected between vitamin E and selenium in experimental studies, these two agents may have reciprocal sparing effects on each other’s requirements [7]. Vitamin E-mediated protection of lipid membranes may spare the requirement for glutathione peroxidase by reducing free radicals at the cell membrane, thereby preventing the leakage of free radicals into the cytosol.

HD patients have a high OxS that is correlated with the total time on dialysis [12]. Although vitamin E status is generally not impaired among HD patients, its oral administration at a high dose of 1200 IU 6h before haemodialysis has already been shown to attenuate intra-dialysis OxS. HD patients often have reduced blood selenium and glutathione peroxidase concentrations [13]. However, selenium supplementation has failed to increase plasma antioxidant activity in these patients [11,13]. This is largely because the kidneys that are the major sources of plasma glutathione peroxidase have already lost their function in HD patients [11]. In a previous study, it has been postulated that selenium supplementation increases red blood cell glutathione peroxidase activity but not that of plasma [11].

Intravenous ferrotherapy is also associated with increased risk of bacterial infection in HD patients [14]. It has been shown that parenteral iron markedly increases plasma and renal monocyte chemotactant protein-1 and may induce inflammation [15]. Immuno-modulatory properties of vitamin E and selenium may further add to its efficacy in dialysis patients. Finally, a single oral dose of vitamin E (400 IU) and selenium (600 μg), taken 6h before a dialysis session, can markedly reduce intra-dialysis OxS in HD patients receiving iron infusion.

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Conflict of interest statement. None declared.

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Pharmacokinetics of bevacizumab in haemodialysis

Sir,

Bevacizumab, a recombinant humanized monoclonal antibody against VEGF (rhuMAb VEGF, Avastin®, Genentech, South San Francisco, CA), was approved as a treatment for metastatic renal cell carcinoma (RCC) [1]. However, no bevacizumab pharmacokinetic data are available for patients with renal failure. We report a pharmacokinetic study of bevacizumab in a patient with renal insufficiency requiring haemodialysis.

Bevacizumab was instituted at a dose of 5 mg/kg every 2 weeks for a 23-year-old patient with mRCC. Bevacizumab serum concentrations were determined after 6 months of treatment, in a pharmacokinetic study over 2 weeks.

Blood samples were collected just before and after the end of infusion. Additional blood samples were collected over the dosing interval before, during and after dialysis sessions. Paired arterial and venous blood samples were performed simultaneously 2 h after the start of haemodialysis. Haemodialysis was performed for 4 h using a F60 polycrylonitrile dialyser (surface area 1.6 m2) every 2 days with a double-needle access to a radial arteriovenous fistula with a constant dialysate flow rate of 500 ml/min and a blood flow rate of 250–300 ml/min.

Bevacizumab serum and dialysate concentrations were measured using an ELISA technique. Bevacizumab pharmacokinetics were analysed by both a non-parametric and a compartmental approach using WinNonLin software (Pharsight Corporation). Pharmacokinetic parameters obtained for our patient were compared with those of subjects with normal renal function [2] receiving 10 mg/kg twice monthly, his bevacizumab area under the curve (AUC) was twice lower than published values (45205 vs 97488 mg h/ml, respectively). Since his pharmacokinetic parameters were equivalent to those of patients with normal renal function, we think that the dose of 5 mg/kg would be adapted to the haemodialysed patient. Furthermore, bevacizumab seems not to be dialysable and administration may, thus, be performed anytime before or after the session on haemodialysis days.


Table 1. Pharmacokinetic parameters of bevacizumab in a haemodialysed patient

<table>
<thead>
<tr>
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<th>Reference values at steady state in patient with normal renal function</th>
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<td>Dosing interval (day)</td>
<td>14</td>
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<tr>
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<td></td>
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</tr>
<tr>
<td>Clmax (µg/ml)</td>
<td>206</td>
<td>284</td>
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<tr>
<td>Cmin (µg/ml)</td>
<td>80</td>
<td>NA</td>
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<td>T1/2 (days)</td>
<td>11.9</td>
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<td>CL/F (ml/min)</td>
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<tr>
<td>Vd (l)</td>
<td>2.52</td>
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<td>Haemodialysis E (%)</td>
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CHFH: haemodialysis clearance: [(Ca–Cv) x Qb]/Ca; Ca: concentration entering the dialyser (ng/ml); Cv: concentration leaving the dialyser (ng/ml); Qb: blood flow (ml/min); E: extraction coefficient (%); CLHD/Qb; FH (%) = CLHD/[CLHD + CLnonHD] × 100; CLnonHD: total body clearance of the drug on a nonhaemodialysis day (NHDD); NA: not available.

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Pancreatitis and pancreatic abscess in a CAPD patient with severe malnutrition

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